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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/551,301	07/12/2006	Christopher R. Trotta	10589-013-999	4617

20583 7590 12/09/2009

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ART UNIT	PAPER NUMBER
1639	

MAIL DATE	DELIVERY MODE
12/09/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/551,301	TROTTA, CHRISTOPHER R.	
	Examiner	Art Unit	
	CHRISTIAN BOESEN	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 September 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *55-57,63-74,76-79,81,82 and 91-95* is/are pending in the application.

4a) Of the above claim(s) *57,64,66,68,70,72,74,76 and 77* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *55,56,63,65,67,69,71,73,78,79,81,82 and 91-95* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *09/10/2009*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This Non-Final Office Action is responsive to the communication received 09/10/2009.

Claim Status

Claim(s) 1-54, 58-62, 75, 80 and 83-90 have been canceled as filed on 09/10/2009.

Claim(s) 91-95 have been added as filed on 09/10/2009.

Claim(s) 76-78 have been amended as filed on 09/10/2009.

Claim(s) 55-57, 63-74, 76-79, 81-82 and 91-95 are currently pending.

Claim(s) 57, 64, 66, 68, 70, 72, 74 and 76-77 have been withdrawn.

Claim(s) 55-56, 63, 65, 67, 69, 71, 73, 78-79, 81-82 and 91-95 are being examined in this application.

Election/Restrictions

Applicant's election with traverse in the reply filed on 02/17/2009 of group I, claims 55-57, 63-74, 77-79 and 81-82 is noted. New/amended claims 76-78 and 91-95 are grouped with the elected group I invention.

Priority

This application for patent is filed under 35 U.S.C 371 of PCT/US04/09572 (filed on 03/26/2004).

Applicant's claim for the benefit of a prior-filed application under 35 U.S.C. 119(e) or under 35 U.S.C. 120, 121, or 365(c) is acknowledged. Acknowledgment is made for priority to a provisional application 60/458,079 03/27/2003.

Information Disclosure Statement

The information disclosure statement (IDS) submitted on 09/10/2009 is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement has been considered by the Examiner.

Claim Rejection(s) Withdrawn

Upon further consideration, the following claim rejection(s) as set forth in the previous office action is(are) withdrawn:

1. Claims 55-56, 58, 63, 65, 67, 69, 71, 73, 75, 78-79, and 81-82 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 26-48 of copending Application No. 10/551,300.

Claim Rejection(s) Maintained

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 55-56, 65, 67, 71, and 73 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tocchini-Valentini (WO 01/92463; 12/6/2001; Cited in IDS of 01/09/2007), in combination with Gontarek (WO 00/67580; 11/16/2000; Cited in IDS of 12/27/2007).

The claims are drawn to a method for identifying a compound that modulates animalia tRNA splicing endonuclease activity, the method comprising: contacting a compound or a member of a library of compounds with an animalia tRNA splicing endonuclease and a substrate for tRNA splicing endonuclease comprising a nucleic acid, wherein the nucleic acid comprises a tRNA intron within a bulge-helix-bulge structure or a mature domain of a precursor tRNA; and detecting the amount of substrate cleaved, wherein a compound that modulates animalia tRNA splicing endonuclease activity is identified if the amount of substrate cleaved in the presence of a compound is altered relative to the amount of substrate cleaved in the absence of the compound or in the presence of a negative control.

Tocchini-Valentini teaches methods of monitoring tRNA splicing endonuclease activity on various target molecules (see claims 1-17 and examples 1-3). Tocchini-Valentini teaches cleaving the mature domain of a tRNA molecule with the purified form (*in vitro*) and *in vivo* form animalia endonuclease (*Xenopus laevis* and murine NIH3T3 cells) (see pages 13-22 and figures 1-3). Tocchini-Valentini teaches contacting a substrate for tRNA splicing endonuclease with a tRNA splicing endonuclease (see pages 6-8 and figures 1-10). Tocchini-Valentini teaches the substrate contains bulge-helix-bulge or mature domain structure (see page 6, example 1, and figure 5). Tocchini-Valentini teaches detecting the amount of substrate cleaved (see page.7,

example 2, figure 3, claims 1-17), which reads on the detecting substrate cleaved present step (b) of claim 55. The reference also teaches linking a fluorescent label with the nucleic acid substrate (e.g. GFP) (see pages 4 and 25 and figure 5). Tocchini-Valentini teaches detecting the GFP expression as an indication of the endonuclease activity (see page 25 and figure 6).

Tocchini-Valentini does not teach assaying for a compound that can reduce (or inhibit) RNA splicing.

However, Gontarek teaches methods or assays for screening for a compound that modulate splicing reactions. (see pages 11-13 and 21-26 and claims 1-16). Gontarek teaches contacting a compound to a splicing reaction to inhibit the splicing reaction (see page 2 and claim 1). The reference also teaches how the method of screening compounds can be used to identify inhibitors of splicing polypeptides compounds (see page 23).

It would have been *prima facie* obvious for one of ordinary skill in the art at the time the invention was made to provide Gontarek's methods of identifying a compound that modulates Tocchini-Valentini's animalia tRNA splicing endonuclease activity, comprising contacting a compound with a animalia tRNA splicing endonuclease and a substrate for tRNA splicing endonuclease, and comprising detecting the amount of substrate cleaved to arrive at applicant's invention with the above cited references before them.

A person of ordinary skill in the art would have been motivated to contact Tocchini-Valentini's animalia tRNA splicing endonuclease with compounds of interest to measure the amount of RNA splicing, because Gontarek teaches that tRNA splicing endonuclease reactions are useful for screening for compounds that inhibit the RNA splicing mechanism.

A person of ordinary skill in the art would have reasonable expectation of success to screen for compounds that modulate animalia tRNA splicing endonuclease activity because the tools to execute this method were available to the skilled artisan as evidenced by Tocchini-Valentini's and Gontarek.

Thus the present invention would have been *prima facie* obvious at the time the invention was made.

Discussion and Answer to Argument

Applicant's arguments have been fully considered but they are not persuasive for the following reasons (in addition to reasons of record). Each point of Applicant's traversal is addressed below (Applicant's arguments are in italic):

Applicants assert "There is no teaching or suggestion in Tocchini-Valentini that tRNA splicing endonuclease may be used as a drug target and to screen for compounds that modulate the activity of animalia tRNA splicing endonuclease." (Reply page 10 center).

Applicants traversed the above rejection over the combination of the cited references by traversing the Tocchini-Valentini reference alone. In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

Applicants are respectfully directed to the body of the rejection above for detailed discussion of how the combination of the cited references teaches all elements and renders the instant claimed invention obvious.

Further, applicants are also respectfully directed to the Supreme Court decision, which forecloses the argument that a specific teaching, suggestion, or motivation is required in the references to support a finding of obviousness. *KSR, 127 S.Ct. at 1741, 82 USPQ2d at 1396.*

Applicants also argue the Gontarek reference teaches screening for compound that modulate animalia pre-mRNA splicing (not tRNA splicing), and thus the cited references cannot be combined because "there are fundamental differences between mRNA splicing and tRNA splicing" (Reply page 11 center+).

Applicants also assert *"one of ordinary skill in the art to substitute one splicing pathway for another" (Reply page 11 center).* The above rejection over the combination of cited reference does not rely on the reasoning that one can simply substitute one RNA splicing pathway for the other. Applicants are respectfully directed to the above rejection for the reasoning statements to combine the references. The instant claim is drawn to a screening method with the steps of detecting tRNA splicing in the presence of a compound (which the compound can be any compound). The instant claimed screening method is similar to any compound screening method, where compounds are contacted with a reaction/assay mixture (such as a tRNA splicing reaction mixture or cell containing the splicing components). The detailed mechanism of how the splicing actually occurs, in a sense, is irrelevant to the screening assay. That is as long as the components in a reaction/assay (such as a tRNA splicing reaction) are known and the assay system has been

demonstrated to produce observable outcome (the spliced tRNA substrate), one of skill in the art can simply add testing compounds to the assay system and determine the effect of the compound (i.e. production or inhibition of the splicing reaction). Applicants have not provided any evidence to show that adding compounds to tRNA splicing assay to detect the effect of the compounds is highly unpredictable. Although there are differences in mRNA and tRNA splicing, applicants have not demonstrated how the difference would render the screening assay inoperable.

In fact, the state of the art supports the predictability of screening compounds for various RNA processing events. For example, Rana (04/12/2001 PCT Patent Application Publication WO 01/25486 A1), throughout the publication teach general methods/assays for identifying RNA binding compounds. The reference teaches by identifying RNA binding compounds, compounds that can inhibit RNA-protein interaction (i.e. inhibit RNA processing events depending on the protein). The reference also teaches the assay or screening methods are applicable to identify compounds involved in various tRNA processes. As pointed out by applicants (*Reply page 11 bottom+*), at least one common mechanism, protein binding to RNA, would be required for both mRNA and tRNA splicing. That is the tRNA endonuclease must bind to the tRNA for the reaction to occur. It would be predictable to screen for compounds that would inhibit such interaction.

Therefore, it would have been obvious to a person of ordinary skill in the art to try various combinations of the known methods of screening for compounds of interested based their abilities to inhibit RNA splicing in cells, methods of detecting RNA splicing using tRNA splicing endonuclease with the appropriate substrate, etc., in an attempt to optimize and/or

improve the screening method of detecting RNA splicing inhibitors in cells, as a person with ordinary skill has good reason to pursue the known options within his or her technical grasp.

Applicants also assert "Neither Tocchini-Valentini nor Gontarek provide any indication that an animalia tRNA splicing endonuclease might be a suitable drug target." (Reply page 13 center).

However, the instant claims are not drawn to a method that require the compounds to be used as a "drug target." In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., "drug target") are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Regardless whether or not tRNA splicing endonuclease can be a suitable drug target, one of skilled in the art would be motivated to test for compounds that would modulates (or inhibit) the tRNA splicing endonuclease because the identified compounds would at least provide a useful research tool for studying the tRNA splicing mechanism.

Claims 63, 69, and 73 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tocchini-Valentini (WO 01/92463; 12/6/2001; Cited in IDS of 01/09/2007), in combination with Gontarek (WO 00/67580; 11/16/2000; Cited in IDS of 12/27/2007) as applied to claim 55 and further in view of Marras (Nucleic Acids Research 2002 vol 30 pp 1-8).

Tocchini-Valentini teaches methods of monitoring tRNA splicing endonuclease activity on various target molecules (see claims 1-17 and examples 1-3). Tocchini-Valentini teaches cleaving the mature domain of a tRNA molecule with the purified form (*in vitro*) and *in vivo* form animalia endonuclease (*Xenopus laevis* and murine NIH3T3 cells) (see pages 13-22 and figures 1-3). Tocchini-Valentini teaches contacting a substrate for tRNA splicing endonuclease with a tRNA splicing endonuclease (see pages 6-8 and figures 1-10). Tocchini-Valentini teaches the substrate contains bulge-helix-bulge or mature domain structure (see page 6, example 1, and figure 5). Tocchini-Valentini teaches detecting the amount of substrate cleaved (see page.7, example 2, figure 3, claims 1-17), which reads on the detecting substrate cleaved present step (b) of claim 55. The reference also teaches linking a fluorescent label with the nucleic acid substrate (e.g. GFP) (see pages 4 and 25 and figure 5). Tocchini-Valentini teaches detecting the GFP expression as an indication of the endonuclease activity (see page 25 and figure 6).

Tocchini-Valentini does not teach assaying for a compound using a nucleic acid labeled with a fluorophore and quencher.

However, Marras teaches labeling nucleic acids with a fluorophore and quencher in methods of nucleic acid detection (see entire document). Marras also teaches labeling the nucleic acid at the 5' end with a fluorophore and at the 3' end with a quencher (see page 2 and figures 1 and 2).

It would have been *prima facie* obvious for one of ordinary skill in the art at the time the invention was made to label Tocchini-Valentini's nucleic acids with Marras's fluorophore and quencher to arrive at applicant's invention with the above cited references before them.

A person of ordinary skill in the art would have been motivated to label Tocchini-Valentini's nucleic acids with Marras's fluorophore and quencher because Marras teaches nucleic acid detection using quenchers in combination with fluorophores allow for generation of a fluorescent signal from an efficient energy transfer.

A person of ordinary skill in the art would have reasonable expectation of success to detect cleaved tRNA labeled with a fluorophore and quencher because the labeling of nucleic acids was available to the skilled artisan at the time of the invention as evidenced by Marras.

Thus the present invention would have been *prima facie* obvious at the time the invention was made.

Discussion and Answer to Argument

Applicant's arguments have been fully considered but they are not persuasive for the following reasons (in addition to reasons of record). Each point of Applicant's traversal is addressed below (Applicant's arguments are in italic):

"The claims are thus not directed to oligonucleotide probes or hybridization assays. Marras does not teach or even suggest a nucleic acid substrate comprising a tRNA intron...." (Reply page 14 bottom).

In response to Applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

Applicants traversed the above rejection over the combination of the cited references by traversing the Marras reference alone. Applicants are respectfully directed to the body of the rejection above for detailed discussion of how the combination of the cited references teaches all elements and renders the instant claimed invention obvious.

Further, applicants are also respectfully directed to the Supreme Court decision, which forecloses the argument that a specific teaching, suggestion, or motivation is required in the references to support a finding of obviousness. *KSR, 127 S.Ct. at 1741, 82 USPQ2d at 1396.*

The splicing of RNA results in a change in two and three dimensional structure. This change in structure results in new locations of nucleotides relative to each other. RNA hybridization results in the formation of the tRNA structure. The new location of nucleotides creates the opportunity for the generation or loss of a signal. The hybridization of two different stands of DNA to form a double stranded DNA molecule also results in a change in two and three dimensional structure and results in new locations of nucleotides relative to each other. Marras teaches nucleic acid detection when a change in structure results in new locations of nucleotides relative to each other. Marras teaches this is a useful method because it is energy efficient because using quenchers in combination with fluorophores allow for generation of a fluorescent signal from an efficient energy transfer.

Claims 78-79, and 81-82 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tocchini-Valentini (WO 01/92463; 12/6/2001; Cited in IDS of 01/09/2007), in combination with Gontarek (WO 00/67580; 11/16/2000; Cited in IDS of 12/27/2007) as

applied to claim 55 and further in view of Herrenknecht (Nucleic Acids Research 1988 vol 16 pp 7713-7714).

Tocchini-Valentini teaches methods of monitoring tRNA splicing endonuclease activity on various target molecules (see claims 1-17 and examples 1-3). Tocchini-Valentini teaches cleaving the mature domain of a tRNA molecule with the purified form (*in vitro*) and *in vivo* form animalia endonuclease (*Xenopus laevis* and murine NIH3T3 cells) (see pages 13-22 and figures 1-3). Tocchini-Valentini teaches contacting a substrate for tRNA splicing endonuclease with a tRNA splicing endonuclease (see pages 6-8 and figures 1-10). Tocchini-Valentini teaches the substrate contains bulge-helix-bulge or mature domain structure (see page 6, example 1, and figure 5). Tocchini-Valentini teaches detecting the amount of substrate cleaved (see page.7, example 2, figure 3, claims 1-17), which reads on the detecting substrate cleaved present step (b) of claim 55. The reference also teaches linking a fluorescent label with the nucleic acid substrate (e.g. GFP) (see pages 4 and 25 and figure 5). Tocchini-Valentini teaches detecting the GFP expression as an indication of the endonuclease activity (see page 25 and figure 6).

Tocchini-Valentini does not teach using human tRNA splicing endonuclease.

Herrenknecht teaches an extract containing human tRNA splicing endonuclease in the method of *in vitro* pre-tRNA splicing (see entire document).

It would have been *prima facie* obvious for one of ordinary skill in the art at the time the invention was made to substitute Tocchini-Valentini's mouse tRNA splicing endonuclease with Herrenknecht's human tRNA splicing endonuclease to arrive at applicant's invention with the above cited references before them.

The present claims would have been obvious because the substitution of one known element human tRNA splicing endonuclease, taught by Herrenknecht for another mouse tRNA splicing endonuclease, taught by Tocchini-Valentini would have yielded predictable results to one of ordinary skill in the art at the time of the invention (i.e. modulating human tRNA splicing endonuclease). See *KSR International Co. v. Teleflex Inc.*, 82 USPQ2d 1385 (U.S. 2007).

Thus the present invention would have been *prima facie* obvious at the time the invention was made.

Discussion and Answer to Argument

Applicant's arguments have been fully considered but they are not persuasive for the following reasons (in addition to reasons of record). Each point of Applicant's traversal is addressed below (Applicant's arguments are in italic):

"Herrenknecht does not teach or suggest screening for compounds that modulate human tRNA splicing endonuclease." (Reply page 15 bottom).

Applicants traversed the above rejection over the combination of the cited references by traversing the Herrenknecht reference alone. In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

Applicants are respectfully directed to the body of the rejection above for detailed discussion of how the combination of the cited references teaches all elements and renders the instant claimed invention obvious.

Further, applicants are also respectfully directed to the Supreme Court decision, which forecloses the argument that a specific teaching, suggestion, or motivation is required in the references to support a finding of obviousness. *KSR, 127 S.Ct. at 1741, 82 USPQ2d at 1396.*

Applicant also argues "Herrenknecht does not provide any indication that a human tRNA splicing endonuclease might be a suitable drug target, in particular suitable target to identify an anti-proliferative drug." (Reply page 15 bottom).

However, the instant claims are not drawn to a method that require the compounds to be used as a "drug target." In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., "drug target") are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Regardless whether or not tRNA splicing endonuclease can be a suitable drug target, one of skilled in the art would be motivated to test for compounds that would modulates (or inhibit) the tRNA splicing endonuclease because the identified compounds would at least provide a useful research tool for studying the tRNA splicing mechanism.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 55-56, 58, 63, 65, 67, 69, 71, 73, 75, 78-79, and 81-82 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 42-64 of copending Application No. 10/551,304.

Although the conflicting claims are not identical, they are not patentably distinct from each other because the present claims and the claims of copending application are drawn to a method a method for identifying a compound that modulates tRNA splicing endonuclease activity comprising contacting a compound with tRNA splicing endonuclease and a substrate and detecting the amount of substrate cleaved. Therefore the present claims are obvious in view of the claims of the copending Application 10/551,304.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Discussion and Answer to Argument

Applicant's arguments have been fully considered but they are not persuasive for the following reasons (in addition to reasons of record). Each point of Applicant's traversal is addressed below (Applicant's arguments are in italic):

Applicants requested the ODP rejection be held in abeyance. Applicants have not provided any specific traversal over the above ODP rejection. Thus, the above rejection is maintained for the reasons of record.

New Necessitated Claim Objection(s) / Rejection(s)

Claim Rejections - 35 USC § 103

Tocchini-Valentini and Others

Claims 55-56, 65, 67, 71, and 73 and 91-95 are rejected under 35 U.S.C. 103(a) as being unpatentable over **Tocchini-Valentini** et al (WO 01/92463; 12/6/2001; Cited in IDS), in view of **Gontarek** (WO 00/67580; 11/16/2000; cited in IDS), and if necessary, in view of **Abelson** (05/22/1998 Journal of Biological Chemistry volume 273 page 12685). This rejection is necessitated by applicant's amendments to the claims.

Tocchini-Valentini et al., throughout the publication, teaches methods of monitoring tRNA splicing endonuclease activity on various target molecules, as discussed supra.

Gontarek, throughout the publication, teaches methods or assays for screening for compound that modulate splicing reactions, as discussed supra.

The combined teaching of the Tocchini-Valentini and Gontarek references as discussed supra are hereby incorporated by reference in its entirety.

The combination of the Tocchini-Valentini and Gontarek references does not explicitly teach using the precursor tRNA has a mature domain as recited in **claims 91-95**.

However, **Abelson** et al., throughout the publication, teach tRNA splicing and the substrates for splicing. The reference specifically teaches using pre-tRNA with "a mature domain" (e.g. p.12685, right col.) The reference also teaches the mature domain is important for proper splicing to occur and it is part of the natural recognition mechanism (e.g. p.12685).

Therefore, it would have been prima facie obvious for one of ordinary skill in the art at the time the invention was made to use a pre-tRNA with a mature domain in a tRNA splicing assay.

A person of ordinary skill in the art would have been motivated at the time of the invention to use a pre-tRNA with a mature domain, because Abelson et al. teach the mature domain is naturally occurring and is needed for proper tRNA splicing recognition. In addition, because the cited references teach methods of tRNA splicing using various substrates, it would have been obvious to one skilled in the art to substitute one substrate for the other (one with a mature domain) to achieve the predictable result of properly splicing pre-tRNA for tRNA splicing assays.

A person of ordinary skill in the art would have reasonable expectation of success of achieving such modifications since the cited references have demonstrated the success of splicing various tRNA substrates.

Conclusion

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to CHRISTIAN BOESEN whose telephone number is 571-270-1321. The Examiner can normally be reached on Monday-Friday 9:00 AM to 5:00 PM.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Christopher S. Low can be reached on 571-272-0951. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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/Christian Boesen/
Examiner, Art Unit 1639

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Primary Examiner, Art Unit 1639